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Short Report: Care Delivery

Diurnal temporal patterns of hypoglycaemia in hospitalized people with diabetes may reveal potentially correctable factors

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Abstract

Aim To determine whether diurnal temporal variations in hypoglycaemic frequency occur in hospitalized patients.

Methods Hypoglycaemic events were identified in a snapshot bedside audit of capillary blood glucose results from diabetes charts of all inpatients receiving insulin or a sulphonylurea (with or without insulin) on 2 days separated by 6 weeks. Additionally, capillary blood glucose measurements were remotely captured over 2 months, in the same category of patients, and analysed for temporal patterns. Hypoglycaemia was defined as 'severe' when the capillary blood glucose was < 3.0 mmol/l and 'mild' when the capillary blood glucose was between 3.0 and 3.9 mmol/l.

Results The bedside audit found that 74% of those audited experienced a hypoglycaemia event. Eighty-three per cent of all hypoglycaemic events and 70% of severe events were recorded between 21.00 and 09.00 h. This was confirmed in the longer duration remote monitoring study where 70% of all hypoglycaemic events and 66% of severe events occurred between 21.00 and 09.00 h.

Conclusion Hypoglycaemia occurs more frequently between 21.00 and 09.00 h in hospitalized patients receiving treatments that can cause hypoglycaemia. This may be related to insufficient carbohydrate intake during this period, and is potentially preventable by changes in catering practice.

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Introduction

Recently, there has been increased focus on achieving good glycaemic control in hospitalized patients, as hyperglycemia is associated with adverse clinical outcomes and early trials demonstrated better outcomes in those randomized to tight control [1–9]. However, hypoglycaemia is a major risk when aiming for tight glucose control. Not only is it unpleasant for the patient, but it is associated with increased length of stay, coma and morbidity [10–12]. Furthermore, recent studies suggest that tight control increases mortality, which may be related to hypoglycaemia [13–18]. Subsequently, the American Diabetes Association and the Endocrine Society recommended a range of 7.8–10.0 mmol/l for critically ill patients and pre-meal targets of 7.8 mmol/l with random results of < 10 mmol/l for non-critical patients [19,20]. Recent Joint British Diabetes Societies guidelines recommend levels between 6.0 and 10 mmol/l [21].

Apart from the underlying illness, barriers to achieving these targets include, clinician inertia, poor understanding of the therapeutic action of the various hypoglycaemic agents and the influence of therapies such as steroids. Nutrition and the timing of meals in relation to therapy are also fundamental. For inpatient staff, concern about precipitating hypoglycaemia is understandably a major barrier, as hypoglycaemia is not infrequent and more alarming than hyperglycaemia. In the UK National Diabetes Inpatient Audit (NaDIA), hypoglycaemia occurred in 23.4% of all inpatients with diabetes and resulted in 2.2% requiring intravenous glucose or parentral glucagon [22].

Preventing inpatient hypoglycaemia requires an understanding of event patterns in the hospital. Having anecdotally observed an increased frequency overnight, we conducted a preliminary bedside snapshot audit, followed by a less labour intensive, but larger study using a remote data management system to explore this.

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What's new?

- The very high frequency of overnight hypoglycaemia is of considerable importance to inpatient diabetes teams.
- Potentially preventable if related to the long interval between the evening meal and breakfast, and the lack of a bedtime snack.
- A follow-up study where a snack is provided should answer this.
- Informal feedback suggests increased nocturnal hypoglycaemia may be a problem in other organizations.
- The audit methods described could be used by other teams to determine whether temporal variations in hypoglycaemic events exist in their organization and whether these relate to specific practices that can be addressed.

Patients and methods

The audits were undertaken by diabetes specialist nurses in the Ipswich Hospital, an acute hospital of 550 inpatient beds.

The snapshot bedside audit

All capillary blood glucose results recorded on the bedside diabetes charts of inpatients with a minimum stay exceeding 24 h were included in the audit, which was conducted on two separate days 6 weeks apart. In those whose stay went beyond a week, only the last 7 days were included. Finger-prick capillary blood glucose was estimated using the Precision Xceed Pro™ system (Abbott Diabetes Care Inc., Alameda, CA, USA).

Hypoglycaemia was defined as 'severe' and 'mild' when the capillary blood glucose was < 3.0 mmol/l and between 3.0 and 3.9 mmol/l, respectively. Results of < 4.0 mmol/l within 4 h of a previous hypoglycaemic event were excluded as they could reflect retesting rather than a new event. Patients on diet alone, and those on glucose-lowering therapies not associated with hypoglycaemia, for example, metformin and/or dipeptidyl peptidase (DPP-4) inhibitors were excluded as readings of < 4 mmol/l are unlikely to represent true drug-induced hypoglycaemia. Patients on insulin were tested pre-meal and pre-bed and those on sulphonylureas at least twice daily.

Patients who experienced hypoglycaemia were invited to fill in a short patient experience questionnaire.

Extended audit using a web database

To validate the results of the snapshot audit, a larger patient sample was audited using an electronic remote data capture system over 2 months (September and October 2012). All inpatient capillary blood glucose readings were measured on the Precision Xceed Pro blood glucose meters and relayed to a PrecisionWeb Point-of-Care Data Management System™ (Abbott Diabetes Care Inc.). From this database, all values of < 4.0 mmol/l and their timings were extracted and examined for temporal patterns. The exclusion criteria were the same as in the previous audit.

Results

The snapshot audit

Glucose charts for all 164 patients were reviewed; 55 were excluded for stated reasons. Of the remaining 109, 71 were receiving insulin and 38 a sulphonylurea without insulin. Eighty-one (74%) had one or more values of < 4 mmol/l accounting for 116 events. Ninety-six events (83%) occurred between 21.00 and 09.00 h. The majority of events occurred in insulin-treated patients (59 events; 61%). Severe hypoglycaemia occurred in 43 of 116 events (37%), of which 30 (70%) occurred between 21.00 and 09.00 h.

Extended audit using Abbott PrecisionWeb database

The remote system captured 7660 capillary blood glucose tests in September and 8184 in October. Table 1 shows the combined hypoglycaemic data as well as data for each month. The similarity in both months demonstrates the robustness of the capture method.

Altogether there were 771 values of < 4 mmol/l, representing 4.9% of all 15 844 tests. Four hundred and sixty-four (60%) were mild and 307 (40%) severe; similar to the snapshot audit.

Between 09.00 and 21.00 h there were 229 hypoglycaemic readings and 542 between 21.00 and 09.00 h; 2.4 times as

Table 1 Hypoglycaemia events* detected during September and October 2012 and over the whole 8-week period using the automated data collection; period presented per 24 h and divided into two 12-h time periods from 09.00 h

	Events per calendar period		
Time periods	Combined 8 weeks	September 2012	October 2012
All 24 h			
Mild hypoglycaemia	464	237	227
Severe hypoglycaemia	307	149	158
Total hypoglycaemic events	771	386	385
09.00–21.00 h			
Mild hypoglycaemia	126	63	63
Severe hypoglycaemia	103	54	49
Total hypoglycaemic events	229	117	112
21.00–09.00 h			
Mild hypoglycaemia	338	174	164
Severe hypoglycaemia	204	95	109
Total hypoglycaemic events	542	269	273

*Mild hypoglycaemia: < 4 but > 3 mmol/l; severe hypoglycaemia: < 3 mmol/l.

many, accounting for 70% of all hypoglycaemic events. Severe events and mild events were 1.98 and 2.68 times as frequent overnight, respectively; (66 and 73% of all severe and mild events, respectively).

Discussion

Hypoglycaemia is a concern for hospitalized patients with diabetes [10–18]. Many factors contribute, including critical illness, alteration in medications—such as rapid steroid reduction, emesis, reduced oral intake, fasting for procedures, impaired mental state as a result of sedation or illness, and interruption of glucose infusions, enteral or parentral nutrition [19]. Arguably, the most important relates to matching the timing and dose of such therapy, especially insulin, to the time and size of the meals. Although well recognized by diabetes staff, the importance of this is not always appreciated by other clinical and catering staff.

In both audits more than two-thirds of hypoglycaemic events occurred between 21.00 and 09.00 h; indeed, this may be an underestimate, as glucose testing is less frequent overnight. Furthermore, hypoglycaemia is more likely to be recognized and documented during the day as it may go unrecognized during sleep if mild and asymptomatic. Indeed, in the home setting, McNally *et al.* found symptomatic hypoglycaemia to be more frequent in the day, but, using continuous glucose monitoring, hypoglycaemia was found to be more frequent in the night [23]. In contrast, in the Diabetes Control and Complications Trial (DCCT), severe symptomatic events were more common in the night [24].

We speculate that the pattern seen in our organization could be explained by patients being subjected to a prolonged fast, the evening meal being served around 17.00 h and breakfast around 08.30 h, without an intervening bedtime snack. Mistiming of insulin to meals, which occurs frequently in hospital, is potentially another factor; however, it was not possible to assess the magnitude of this. For many reasons, patients lose control of their glycaemic treatments to clinical staff, but the inability to influence the content, size and timing of meals may be of greater importance than the clinical decisions around hypoglycaemic medications. Furthermore, the loss of freedom to snack whenever required may deny patients of a vital preventative measure. It is of interest that, when questioned, 68% who had experienced inpatient hypoglycaemia stated that this was their first 'hypo', suggesting that self-management, particularly by those with Type 2 diabetes had previously prevented it.

To establish whether this pattern was specific to our hospital, we conducted an e-mail poll of eighteen diabetes inpatient nurses from different hospitals in England. All reported a 14- to 15-h gap between the evening meal and breakfast. Unaware of our findings, 14 nurses reported hypoglycaemia to be more common overnight, of whom 12 said a bedtime snack was never or only sometimes available. In contrast, three of the four that did not notice increased nocturnal hypoglycaemia said a bedtime snack was always available. Ten of the 14 nurses reporting temporal patterns had concerns with one or more of the size, content and timing of meals, whereas only one of the four who did not notice a pattern had such issues. Of relevance, in the National Diabetes Inpatient Audit, the commonest area of patient dissatisfaction related to meals. Furthermore, those reporting such dissatisfaction were twice as likely to have experienced severe hypoglycaemia [22].

Previous publications of in-hospital remote glucose monitoring report a hypoglycaemia frequency of 3.3–5.7%, not dissimilar to the 4.9% we observed [25–27]. It should be noted that this relates to results in the hypoglycaemic range as a percentage of all capillary blood glucose tests, rather than hypoglycaemic risk for an individual. The snapshot audit showed an alarming 74% of patients had a hypoglycaemic episode and, although greater, is in keeping with the findings of the National Diabetes Inpatient Audit, where 70.9% of subjects with Type 1 diabetes and 47.5% of subjects with Type 2 diabetes who were insulin treated experienced hypoglycaemia [22].

As far as we are aware, there has been only one previous report, from a small US hospital, of more frequent hypoglycaemia overnight [28]. Our study adds to this evidence, but also suggests that, at least for our hospital, this may be related to an institutional practice that can be addressed.

In conclusion, by exploring daily temporal patterns of blood glucose readings in hospitalized patients, we found hypoglycaemia to be more frequent during the night. We believe this relates to timing and content of meals and the lack of evening snacks. Although not proven, feedback from patients and other hospitals supports this. These nutritional issues are being addressed and the outcome will be assessed in an ongoing audit. We recommend that other organizations undertake a similar exercise to determine whether temporal variations in hypoglycaemic events exist in their hospitals and whether these relate to specific practices that can be addressed.

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None.

Competing interests

None declared.

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